087,188

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* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS 1		Web Page URLs for STN Seminar Schedule - N. America
NEWS 2		"Ask CAS" for self-help around the clock
NEWS 3	JAN 27	Source of Registration (SR) information in REGISTRY updated and searchable
NEWS 4	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAplus
NEWS 5	FEB 05	German (DE) application and patent publication number format changes
NEWS 6	MAR 03	MEDLINE and LMEDLINE reloaded
NEWS 7	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS 8	MAR 03	FRANCEPAT now available on STN
NEWS 9	MAR 29	Pharmaceutical Substances (PS) now available on STN
NEWS 10	MAR 29	WPIFV now available on STN
NEWS 11	MAR 29	No connect hour charges in WPIFV until May 1, 2004
NEWS 12	MAR 29	New monthly current-awareness alert (SDI) frequency in RAPRA

NEWS EXPRESS	MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 13 APRIL 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 16:25:44 ON 23 APR 2004

=> file ca

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'CA' ENTERED AT 16:25:53 ON 23 APR 2004
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FILE COVERS 1907 - 22 Apr 2004 VOL 140 ISS 18
FILE LAST UPDATED: 22 Apr 2004 (20040422/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s alpha(W)2(W)macroglob?
       1448060 ALPHA
          2473 ALPHAS
       1448150 ALPHA
                  (ALPHA OR ALPHAS)
       7818176 2
          8809 MACROGLOB?
L1        5767 ALPHA(W)2(W)MACROGLOB?

=>  s alpha(W))sub(W)2(W)macroglob?
MISSING TERM 'W))SUB'
The search profile that was entered contains a logical operator
followed immediately by a right parenthesis ')'.

=> s alpha(W)sub(W)2(W)macroglob?
       1448060 ALPHA
          2473 ALPHAS
       1448150 ALPHA
                  (ALPHA OR ALPHAS)
         64780 SUB
           124 SUBS
         64896 SUB
                  (SUB OR SUBS)
       7818176 2
          8809 MACROGLOB?
L2           0 ALPHA(W)SUB(W)2(W)MACROGLOB?

=> s a2m
L3         262 A2M

=> s a2mg
L4          10 A2MG

=> s a(W)sub(W)2(W)mg
      17183497 A
         64780 SUB
           124 SUBS
         64896 SUB
                  (SUB OR SUBS)
       7818176 2
       1269680 MG
          1182 MGS
       1270439 MG
                  (MG OR MGS)
```

```
L5            0 A(W)SUB(W)2(W)MG

=> s a(W)sub(W)2(W)m
      17183497 A
         64780 SUB
           124 SUBS
         64896 SUB
                  (SUB OR SUBS)
       7818176 2
       2085474 M
L6            1 A(W)SUB(W)2(W)M

=> s l1 or l3 or l4 or l6
L7         5911 L1 OR L3 OR L4 OR L6

=> save temp l7
ENTER NAME OR (END):alpha2mg/a
ANSWER SET L7 HAS BEEN SAVED AS 'ALPHA2MG/A'

=> s Hyaluronic(W)acid
          12105 HYALURONIC
              1 HYALURONICS
          12105 HYALURONIC
                  (HYALURONIC OR HYALURONICS)
        3767545 ACID
        1417285 ACIDS
        4227071 ACID
                  (ACID OR ACIDS)
L8        11528 HYALURONIC(W)ACID

=> s hyaluronan
           2742 HYALURONAN
             33 HYALURONANS
L9         2743 HYALURONAN
                  (HYALURONAN OR HYALURONANS)

=> s hyaluronate
           5608 HYALURONATE
            141 HYALURONATES
L10        5637 HYALURONATE
                  (HYALURONATE OR HYALURONATES)

=> s l8 or l9 or l10
L11       15710 L8 OR L9 OR L10

=> save temp  l11
ENTER NAME OR (END):hyaluronic/a
ANSWER SET L11 HAS BEEN SAVED AS 'HYALURONIC/A'

=> s tissue(W)inhibitor(W)metalloproteinase(W)1
         582962 TISSUE
         288570 TISSUES
         744198 TISSUE
                  (TISSUE OR TISSUES)
         431318 INHIBITOR
         452099 INHIBITORS
         695180 INHIBITOR
                  (INHIBITOR OR INHIBITORS)
          13788 METALLOPROTEINASE
           6934 METALLOPROTEINASES
          15195 METALLOPROTEINASE
                  (METALLOPROTEINASE OR METALLOPROTEINASES)
        7642351 1
```

```
L12          42 TISSUE(W)INHIBITOR(W)METALLOPROTEINASE(W)1

=> s timp1
L13         677 TIMP1

=> s timp(W)1
           3979 TIMP
            961 TIMPS
           4065 TIMP
                  (TIMP OR TIMPS)
        7642351 1
L14        2340 TIMP(W)1

=> s l12 or l13 or l15
L15 NOT FOUND
The L-number entered could not be found.  To see the definition
of L-numbers, enter DISPLAY HISTORY at an arrow prompt (=>).

=> s l12 or l13 or l14
L15        2475 L12 OR L13 OR L14

=> save temp l15
ENTER NAME OR (END):timp1/a
ANSWER SET L15 HAS BEEN SAVED AS 'TIMP1/A'

=> d his

     (FILE 'HOME' ENTERED AT 16:25:44 ON 23 APR 2004)

     FILE 'CA' ENTERED AT 16:25:53 ON 23 APR 2004
L1          5767 S ALPHA(W)2(W)MACROGLOB?
L2             0 S ALPHA(W)SUB(W)2(W)MACROGLOB?
L3           262 S A2M
L4            10 S A2MG
L5             0 S A(W)SUB(W)2(W)MG
L6             1 S A(W)SUB(W)2(W)M
L7          5911 S L1 OR L3 OR L4 OR L6
                 SAVE TEMP L7 ALPHA2MG/A
L8         11528 S HYALURONIC(W)ACID
L9          2743 S HYALURONAN
L10         5637 S HYALURONATE
L11        15710 S L8 OR L9 OR L10
                 SAVE TEMP  L11 HYALURONIC/A
L12           42 S TISSUE(W)INHIBITOR(W)METALLOPROTEINASE(W)1
L13          677 S TIMP1
L14         2340 S TIMP(W)1
L15         2475 S L12 OR L13 OR L14
                 SAVE TEMP L15 TIMP1/A

=> s l7 and l11 and l15
L16            1 L7 AND L11 AND L15

=> activate livfib/a
L17 (    524116)SEA FILE=CA ABB=ON  PLU=ON  HEPATIC OR LIVER OR BILIARY
L18 (     33222)SEA FILE=CA ABB=ON  PLU=ON  FIBROT? OR FIBROS? OR FIBROL? OR FI
L19         3847 SEA FILE=CA ABB=ON  PLU=ON  L17(2A)L18

=> l16 and l19
L16 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).
```

```
=> s l16 and l19
L20             1 L16 AND L19

=> file biosis
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                    56.42      56.63

FILE 'BIOSIS' ENTERED AT 16:37:05 ON 23 APR 2004
COPYRIGHT (C) 2004 BIOLOGICAL ABSTRACTS INC.(R)

FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 21 April 2004 (20040421/ED)

FILE RELOADED: 19 October 2003.

=> s l20
        621255 ALPHA
           373 ALPHAS
        621386 ALPHA
                  (ALPHA OR ALPHAS)
       3031817 2
          7194 MACROGLOB?
          5011 ALPHA(W)2(W)MACROGLOB?
           264 A2M
             8 A2MG
       7620897 A
         58854 SUB
            49 SUBS
         58900 SUB
                  (SUB OR SUBS)
       3031817 2
        678159 M
             0 A(W)SUB(W)2(W)M
          6835 HYALURONIC
             1 HYALURONICS
          6836 HYALURONIC
                  (HYALURONIC OR HYALURONICS)
       1154009 ACID
        308426 ACIDS
       1292321 ACID
                  (ACID OR ACIDS)
          6813 HYALURONIC(W)ACID
          3182 HYALURONAN
            23 HYALURONANS
          3188 HYALURONAN
                  (HYALURONAN OR HYALURONANS)
          2543 HYALURONATE
            30 HYALURONATES
          2554 HYALURONATE
                  (HYALURONATE OR HYALURONATES)
        622816 TISSUE
        248440 TISSUES
        783223 TISSUE
                  (TISSUE OR TISSUES)
        365456 INHIBITOR
        181726 INHIBITORS
        471081 INHIBITOR
                  (INHIBITOR OR INHIBITORS)
         16681 METALLOPROTEINASE
```

```
          8005 METALLOPROTEINASES
         19214 METALLOPROTEINASE
                 (METALLOPROTEINASE OR METALLOPROTEINASES)
       3099252 1
            27 TISSUE(W)INHIBITOR(W)METALLOPROTEINASE(W)1
           169 TIMP1
          4302 TIMP
          1006 TIMPS
          4499 TIMP
                 (TIMP OR TIMPS)
       3099252 1
          2632 TIMP(W)1
        141949 HEPATIC
           510 HEPATICS
        142372 HEPATIC
                 (HEPATIC OR HEPATICS)
        458396 LIVER
         23714 LIVERS
        463052 LIVER
                 (LIVER OR LIVERS)
         36662 BILIARY
          5829 FIBROT?
         73486 FIBROS?
           898 FIBROL?
          3799 FIBROG?
          6903 L17(2A)L18
L21          3 L16 AND L19

=> file medline
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.85      57.48

FILE 'MEDLINE' ENTERED AT 16:37:22 ON 23 APR 2004

 FILE LAST UPDATED: 22 APR 2004 (20040422/UP).  FILE COVERS 1951 TO DATE.

 On February 29, 2004, the 2004 MeSH terms were loaded.  See HELP RLOAD
 for details. OLDMEDLINE now back to 1951.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2004 vocabulary.  See http://www.nlm.nih.gov/mesh/ and
 http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a
 description of changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s l20
        474055 ALPHA
           490 ALPHAS
        474306 ALPHA
                 (ALPHA OR ALPHAS)
       2800372 2
         11808 MACROGLOB?
          4160 ALPHA(W)2(W)MACROGLOB?
           228 A2M
            10 A2MG
       7648522 A
         32058 SUB
            21 SUBS
         32077 SUB
                 (SUB OR SUBS)
```

```
       2800372 2
        375852 M
             0 A(W)SUB(W)2(W)M
         10341 HYALURONIC
       1255858 ACID
        469922 ACIDS
       1453655 ACID
                 (ACID OR ACIDS)
         10325 HYALURONIC(W)ACID
          2644 HYALURONAN
            21 HYALURONANS
          2653 HYALURONAN
                 (HYALURONAN OR HYALURONANS)
          2297 HYALURONATE
            25 HYALURONATES
          2308 HYALURONATE
                 (HYALURONATE OR HYALURONATES)
        761234 TISSUE
        237597 TISSUES
        904488 TISSUE
                 (TISSUE OR TISSUES)
        231337 INHIBITOR
        477753 INHIBITORS
        583190 INHIBITOR
                 (INHIBITOR OR INHIBITORS)
          9649 METALLOPROTEINASE
          8529 METALLOPROTEINASES
         13719 METALLOPROTEINASE
                 (METALLOPROTEINASE OR METALLOPROTEINASES)
       3209923 1
            17 TISSUE(W)INHIBITOR(W)METALLOPROTEINASE(W)1
           112 TIMP1
          3505 TIMP
          1054 TIMPS
          3680 TIMP
                 (TIMP OR TIMPS)
       3209923 1
          2209 TIMP(W)1
        153049 HEPATIC
            16 HEPATICS
        153061 HEPATIC
                 (HEPATIC OR HEPATICS)
        599753 LIVER
         22691 LIVERS
        601239 LIVER
                 (LIVER OR LIVERS)
         55796 BILIARY
            34 BILIARIES
         55806 BILIARY
                 (BILIARY OR BILIARIES)
          6876 FIBROT?
         89303 FIBROS?
          1050 FIBROL?
          3143 FIBROG?
          5128 L17(2A)L18
L22          1 L16 AND L19

=> duplicate remove
ENTER L# LIST OR (END):l20-l21
DUPLICATE PREFERENCE IS 'CA, BIOSIS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):y
ENTER FILE NAMES OF DUPLICATES TO KEEP:ca
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
```

	ENTRY	SESSION
FULL ESTIMATED COST	0.76	58.24

FILE 'CA' ENTERED AT 16:38:41 ON 23 APR 2004
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FILE 'BIOSIS' ENTERED AT 16:38:41 ON 23 APR 2004

PROCESSING COMPLETED FOR L20
PROCESSING COMPLETED FOR L21
L23 4 DUPLICATE REMOVE L20-L21 CA (0 DUPLICATES REMOVED)

=> d l23 1-4 bib ab

L23 ANSWER 1 OF 4 CA
AN 139:242563 CA
TI Macromolecular markers for the diagnosis of **liver fibrosis**
IN Rose, Steven L.; Oh, Esther H.; Walsh, Michael J.
PA Prometheus Laboratories, Inc., USA
SO PCT Int. Appl., 133 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2003073822	A2	20030912	WO 2003-US6038	20030228
	W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2003175686	A1	20030918	US 2002-87188	20020228
PRAI	US 2002-87188	A	20020228		

AB The present invention provides a method of diagnosing the presence or severity of **liver fibrosis** in an individual by detecting **.alpha.2-macroglobulin** (α2-MG) in sample from the individual; detecting **hyaluronic acid** (HA) in a sample from the individual; detecting tissue inhibitor of metalloproteinases-1 (**TIMP-1**) in a sample from the individual; and diagnosing the presence or severity of **liver fibrosis** in the individual based on the presence or level of α2-MG, HA and **TIMP-1**. A number of liver markers were analyzed in serum of patients with **liver fibrosis** of known stages. Statistical analyses of the ability of a number of combinations of markers to accurately discriminate the disease are presented.

PCT pub related to instant application

L23 ANSWER 2 OF 4 BIOSIS
AN 2003:583010 BIOSIS
DN PREV200300572829
TI PERFORMANCE CHARACTERISTICS OF A NON-INVASIVE FIBROSIS MARKER PANEL IN DIFFERENTIATING MINIMAL STAGE (F0-F1) FROM PROGRESSIVELY SEVERE FIBROSIS IN CHRONIC HEPATITIS C PATIENTS. .

AU Patel, Keyur [Reprint Author]
CS Durham, NC, USA
SO Digestive Disease Week Abstracts and Itinerary Planner, (2003) Vol. 2003, pp. Abstract No. M876. e-file.
Meeting Info.: Digestive Disease 2003. FL, Orlando, USA. May 17-22, 2003. American Association for the Study of Liver Diseases; American Gastroenterological Association; American Society for Gastrointestinal Endoscopy; Society for Surgery of the Alimentary Tract.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 10 Dec 2003
Last Updated on STN: 10 Dec 2003
AB Background: Liver biopsy is an invasive and expensive procedure that may be associated with morbidity, but at present provides the only reliable means of assessing disease severity in chronic hepatitis C. There is a need to identify reliable non-invasive serum markers of fibrosis. A panel of markers based on extracellular matrix and connective tissue proteins may have some utility in this regard. Aims: To assess the performance of a 3-marker panel in differentiating minimal fibrosis(F0-F1) from those with severe disease (F4 plus or minus F3) Methods: Serum **hyaluronic acid** (HA), tissue inhibitor of metalloproteinase (**TIMP-1**) and **Alpha-2 macroglobulin** (AMG) had been previously evaluated as a panel of fibrosis markers in 294 selected chronic HCV patients from a single center. An algorithm for METAVIR fibrosis severity (F2/3/4 versus F0/1) was developed, and subsequently validated in 402 chronic HCV patients from another 3 centers. All serum samples were obtained at or near the biopsy date, and stored at minus 70 degrees C. until analysis. Liver biopsies had been scored by an expert panel of pathologists at each center, with a high degree of concordance (0.85) for the METAVIR scoring system. The performance of the panel was evaluated for its ability to distinguish fibrosis stages F4 from F0-F1, and F3-F4 from F0-F1. Results: For all 696 patients the sensitivity of the panel for F2-F4 fibrosis was 60.8 percent, with an accuracy of 79.5 percent. The sensitivity improved to 78.3 percent for F3-F4 (n equals 221) and 89.2 percent for F4 alone (n equals 118). The accuracy of the test was 89.9 percent and 94.5 percent respectively (see table). Specificity of the panel (ie negative test for F0-F1) remained at 96.2 percent. The predictive value of a positive test (PPV) for F3-F4 was 91.8 percent, and 88.1 percent for F4 alone. The indeterminate rates were in the 24-29 percent range (ie panel result that could not be assigned to a fibrosis group). Conclusions: This panel of serum fibrosis markers (FibroSpectSM) may reliably differentiate minimal stage fibrosis from those with bridging fibrosis and cirrhosis in chronic hepatitis C. However, markers that perform well at a moderate fibrosis stage (F2), and which also reflect changes in fibrosis with time, require further evaluation..

L23 ANSWER 3 OF 4 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2003:2943 BIOSIS
DN PREV200300002943
TI Clinical laboratory performance of the FIBROSpectSM serodiagnostic test for the detection of **liver fibrosis**.
AU Oh, Esther H. [Reprint Author]; Nguyen, Philip [Reprint Author]; Mancuso, Rosemary [Reprint Author]; Smith, Katie M. [Reprint Author]
CS Prometheus Laboratories Inc, San Diego, CA, USA
SO Hepatology, (October 2002) Vol. 36, No. 4 Part 2, pp. 566A. print.
Meeting Info.: 53rd Annual Meeting on the Liver. BOSTON, MA, USA. November 01-05, 2002.
ISSN: 0270-9139 (ISSN print).
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English

ED Entered STN: 18 Dec 2002
Last Updated on STN: 18 Dec 2002

L23 ANSWER 4 OF 4 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2004:7174 BIOSIS
DN PREV200400000522
TI Evaluation and optimization of a panel of serum markers for **liver fibrosis** in chronic hepatitis C patients.
AU Patel, Keyur [Reprint Author]; McHutchinson, John G.; Oh, Esther; Nguyen, Phillip; Rose, Steven
CS La Jolla, CA, USA
SO Gastroenterology, (July 2002) Vol. 123, No. 1 Supplement, pp. 48. print.
Meeting Info.: Digestive Disease Week and the 103rd Annual Meeting of the American Gastroenterological Association. San Francisco, CA, USA. May 19-22, 2002. American Gastroenterological Association.
CODEN: GASTAB. ISSN: 0016-5085.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LA English
ED Entered STN: 17 Dec 2003
Last Updated on STN: 17 Dec 2003

post dates

=> d l22 bib ab
YOU HAVE REQUESTED DATA FROM FILE 'MEDLINE' - CONTINUE? (Y)/N:y

L22 ANSWER 1 OF 1 MEDLINE on STN
AN 2003528127 MEDLINE
DN PubMed ID: 14606100
TI Grading and staging of **hepatic fibrosis**, and its relationship with noninvasive diagnostic parameters.
AU Lu Lun-Gen; Zeng Min-De; Wan Mo-Bin; Li Cheng-Zhong; Mao Yi-Min; Li Ji-Qiang; Qiu De-Kai; Cao Ai-Ping; Ye Jun; Cai Xiong; Chen Cheng-Wei; Wang Ji-Yao; Wu Shan-Ming; Zhu Jin-Shui; Zhou Xia-Qiu
CS Shanghai Institute of Digestive Disease, Renji Hospital, Shanghai Second Medical University, Shanghai 200001, China.. lulungen@online.sh.cn
SO World journal of gastroenterology : WJG, (2003 Nov) 9 (11) 2574-8.
Journal code: 100883448. ISSN: 1007-9327.
CY China
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200312
ED Entered STN: 20031108
Last Updated on STN: 20031220
Entered Medline: 20031219
AB AIM: To explore the grade and stage of pathology and the relationship between grading and staging of **hepatic fibrosis** and noninvasive diagnostic parameters. METHODS: Inflammatory activity and **fibrosis** of consecutive **liver** biopsies from 200 patients with chronic liver disease were determined according to the Diagnostic Criteria of Chronic Hepatitis in China, 1995. A comparative analysis was made in these patients comparing serum markers, Doppler ultrasonography, CT and/or MR imaging with the findings of liver biopsy. RESULTS: With increase of inflammatory activity, the degree of fibrosis also rose. There was a close correlation between **liver fibrosis** and inflammatory activity. AST, GGT, albumin, albumin/globulin, ALP, AFP, **hyaluronic acid**, N-terminal procollagen III(P III NP), collagen type IV(Col IV), tissue inhibitors of metalloproteinases-1 (**TIMP-1**), **alpha-2-macroglobulin**, natural killer cells(NK), some parameters of

post dates

Doppler ultrasonography, CT and/or MR imaging were all related to the degree of inflammatory activity. GGT, albumin, albumin/globulin, ALP, AFP, **hyaluronic acid**, Col IV, **TIMP-1**
, alpha-2- macroglobulin, transforming
growth factor-beta 1 (TGFbeta1), NK, some parameters of Doppler ultrasonography, CT and/or MR imaging were all related to the staging of fibrosis. By regression analysis, the parameters used in combination to differentiate the presence or absence of fibrosis were age, GGT, the parameter of blood flow of portal vein per minute, the maximum oblique diameter of right liver by B ultrasound, the wavy hepatic surface contour by CT and/or MR. The sensitivity, specificity and accuracy of the above parameters were 80.36%, 86.67%, and 81.10%, respectively. CONCLUSION: There is close correlation between **liver fibrosis** and inflammatory activity. The grading and staging of **liver fibrosis** are related to serum markers, Doppler ultrasonography, CT and/or MR imaging. The combination of the above mentioned noninvasive parameters are quite sensitive and specific in the diagnosis of **hepatic fibrosis.**

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	1.27	69.30

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	0.00	-0.66

Connection closed by remote host

087,188

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:sssptaul82das

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	JAN 27	Source of Registration (SR) information in REGISTRY updated and searchable
NEWS	4	JAN 27	A new search aid, the Company Name Thesaurus, available in CA/CAplus
NEWS	5	FEB 05	German (DE) application and patent publication number format changes
NEWS	6	MAR 03	MEDLINE and LMEDLINE reloaded
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NEWS EXPRESS	MARCH 31 CURRENT WINDOWS VERSION IS V7.00A, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 13 APRIL 2004
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

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* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 13:33:52 ON 23 APR 2004

=> file ca

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'CA' ENTERED AT 13:34:19 ON 23 APR 2004
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FILE COVERS 1907 - 22 Apr 2004 VOL 140 ISS 18
FILE LAST UPDATED: 22 Apr 2004 (20040422/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s hepatic or liver or biliary
        104129 HEPATIC
            36 HEPATICS
        104155 HEPATIC
                  (HEPATIC OR HEPATICS)
        493900 LIVER
         33502 LIVERS
        496640 LIVER
                  (LIVER OR LIVERS)
         23114 BILIARY
             1 BILIARIES
         23115 BILIARY
                  (BILIARY OR BILIARIES)
L1      524116 HEPATIC OR LIVER OR BILIARY

=> s fibrot? or fibros? or fibrol? or fibrog?
          3134 FIBROT?
         30275 FIBROS?
           528 FIBROL?
          2661 FIBROG?
L2       33222 FIBROT? OR FIBROS? OR FIBROL? OR FIBROG?

=> s l1(2a)l2
L3        3847 L1(2A)L2

=> save temp l3
ENTER NAME OR (END):livfib/a
ANSWER SET L3 HAS BEEN SAVED AS 'LIVFIB/A'

=> s multivariant or multi(W)variant or multiple
           419 MULTIVARIANT
             4 MULTIVARIANTS
           423 MULTIVARIANT
                  (MULTIVARIANT OR MULTIVARIANTS)
         95142 MULTI
             1 MULTIS
         95143 MULTI
                  (MULTI OR MULTIS)
         51165 VARIANT
         52771 VARIANTS
         89749 VARIANT
                  (VARIANT OR VARIANTS)
            40 MULTI(W)VARIANT
        301572 MULTIPLE
```

```
          2810 MULTIPLES
        304080 MULTIPLE
                 (MULTIPLE OR MULTIPLES)
L4      304524 MULTIVARIANT OR MULTI(W)VARIANT OR MULTIPLE

=> s marker or indicator
         99378 MARKER
         87975 MARKERS
        157140 MARKER
                 (MARKER OR MARKERS)
        128101 INDICATOR
         62535 INDICATORS
        170864 INDICATOR
                 (INDICATOR OR INDICATORS)
L5      323438 MARKER OR INDICATOR

=> l4(5a)l5
L4(5A)L5 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l4(5a)l5
L6        1491 L4(5A)L5

=> save temp l6
ENTER NAME OR (END):multmark/a
ANSWER SET L6 HAS BEEN SAVED AS 'MULTMARK/A'

=>  s multivariant or multi(W)variant or multiple or combin?
          419 MULTIVARIANT
            4 MULTIVARIANTS
          423 MULTIVARIANT
                (MULTIVARIANT OR MULTIVARIANTS)
        95142 MULTI
            1 MULTIS
        95143 MULTI
                (MULTI OR MULTIS)
        51165 VARIANT
        52771 VARIANTS
        89749 VARIANT
                (VARIANT OR VARIANTS)
           40 MULTI(W)VARIANT
       301572 MULTIPLE
         2810 MULTIPLES
       304080 MULTIPLE
                (MULTIPLE OR MULTIPLES)
       887119 COMBIN?
L7    1167388 MULTIVARIANT OR MULTI(W)VARIANT OR MULTIPLE OR COMBIN?

=> del l4
L6 REFERENCES L4
DELETE L4? (Y)/N:y

=> s l7(5a)l5
L8        3456 L7(5A)L5

=> del l6
DELETE L6? (Y)/N:y

=> save temp l8
ENTER NAME OR (END):combmark/a
ANSWER SET L8 HAS BEEN SAVED AS 'COMBMARK/A'
```

```
=> d his

     (FILE 'HOME' ENTERED AT 13:33:52 ON 23 APR 2004)

     FILE 'CA' ENTERED AT 13:34:19 ON 23 APR 2004
L1        524116 S HEPATIC OR LIVER OR BILIARY
L2         33222 S FIBROT? OR FIBROS? OR FIBROL? OR FIBROG?
L3          3847 S L1(2A)L2
                 SAVE TEMP L3 LIVFIB/A
L5        323438 S MARKER OR INDICATOR
                 SAVE TEMP L*** MULTMARK/A
L7       1167388 S MULTIVARIANT OR MULTI(W)VARIANT OR MULTIPLE OR COMBIN?
L8          3456 S L7(5A)L5
                 SAVE TEMP L8 COMBMARK/A

=> s detect? or monitor? or diagnos? or prognos?
        1291552 DETECT?
         301921 MONITOR?
         193439 DIAGNOS?
          30923 PROGNOS?
L9      1672622 DETECT? OR MONITOR? OR DIAGNOS? OR PROGNOS?

=> l3 and l8 and l9
L3 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s l3 and l8 and l9
L10           8 L3 AND L8 AND L9

=> file biosis
COST IN U.S. DOLLARS                            SINCE FILE      TOTAL
                                                   ENTRY    SESSION
FULL ESTIMATED COST                                46.46      46.67

FILE 'BIOSIS' ENTERED AT 13:46:13 ON 23 APR 2004
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FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 21 April 2004 (20040421/ED)

FILE RELOADED: 19 October 2003.

=> s l10
         141949 HEPATIC
            510 HEPATICS
         142372 HEPATIC
                  (HEPATIC OR HEPATICS)
         458396 LIVER
          23714 LIVERS
         463052 LIVER
                  (LIVER OR LIVERS)
          36662 BILIARY
           5829 FIBROT?
          73486 FIBROS?
            898 FIBROL?
           3799 FIBROG?
           6903 L1(2A)L2
```

```
            342 MULTIVARIANT
              6 MULTIVARIANTS
            348 MULTIVARIANT
                  (MULTIVARIANT OR MULTIVARIANTS)
          54898 MULTI
              4 MULTIS
          54902 MULTI
                  (MULTI OR MULTIS)
          58932 VARIANT
          54324 VARIANTS
         100435 VARIANT
                  (VARIANT OR VARIANTS)
         312896 MULTIPLE
           1731 MULTIPLES
         314345 MULTIPLE
                  (MULTIPLE OR MULTIPLES)
         572841 COMBIN?
         154381 MARKER
         127559 MARKERS
         249900 MARKER
                  (MARKER OR MARKERS)
          64957 INDICATOR
          37079 INDICATORS
          96884 INDICATOR
                  (INDICATOR OR INDICATORS)
           4935 L7(5A)L5
         929209 DETECT?
         268173 MONITOR?
        1009098 DIAGNOS?
         147652 PROGNOS?
L11          10 L3 AND L8 AND L9

=> file medline
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.85      47.52

FILE 'MEDLINE' ENTERED AT 13:46:46 ON 23 APR 2004

 FILE LAST UPDATED: 22 APR 2004 (20040422/UP).  FILE COVERS 1951 TO DATE.

 On February 29, 2004, the 2004 MeSH terms were loaded.  See HELP RLOAD
 for details. OLDMEDLINE now back to 1951.

 MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the
 MeSH 2004 vocabulary.  See http://www.nlm.nih.gov/mesh/ and
 http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a
 description of changes.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.

=> s l10
         153049 HEPATIC
             16 HEPATICS
         153061 HEPATIC
                  (HEPATIC OR HEPATICS)
         599753 LIVER
          22691 LIVERS
         601239 LIVER
                  (LIVER OR LIVERS)
          55796 BILIARY
             34 BILIARIES
```

```
         55806 BILIARY
                 (BILIARY OR BILIARIES)
          6876 FIBROT?
         89303 FIBROS?
          1050 FIBROL?
          3143 FIBROG?
          5128 L1(2A)L2
           440 MULTIVARIANT
             3 MULTIVARIANTS
           442 MULTIVARIANT
                 (MULTIVARIANT OR MULTIVARIANTS)
         43571 MULTI
            83 MULTIS
         43579 MULTI
                 (MULTI OR MULTIS)
         57141 VARIANT
         49035 VARIANTS
         95277 VARIANT
                 (VARIANT OR VARIANTS)
        403901 MULTIPLE
          3706 MULTIPLES
        405463 MULTIPLE
                 (MULTIPLE OR MULTIPLES)
        703012 COMBIN?
        115121 MARKER
        183060 MARKERS
        258809 MARKER
                 (MARKER OR MARKERS)
         52715 INDICATOR
         83776 INDICATORS
        132020 INDICATOR
                 (INDICATOR OR INDICATORS)
          4690 L7(5A)L5
        821983 DETECT?
        285954 MONITOR?
       1914299 DIAGNOS?
        291133 PROGNOS?
L12          15 L3 AND L8 AND L9

=> duplicate remove
ENTER L# LIST OR (END):l10-l12
DUPLICATE PREFERENCE IS 'CA, BIOSIS, MEDLINE'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/(N):n
COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                         ENTRY    SESSION
FULL ESTIMATED COST                                       0.38      47.90

FILE 'CA' ENTERED AT 13:47:24 ON 23 APR 2004
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FILE 'BIOSIS' ENTERED AT 13:47:24 ON 23 APR 2004
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FILE 'MEDLINE' ENTERED AT 13:47:24 ON 23 APR 2004
PROCESSING COMPLETED FOR L10
PROCESSING COMPLETED FOR L11
PROCESSING COMPLETED FOR L12
L13          22 DUPLICATE REMOVE L10-L12 (11 DUPLICATES REMOVED)

=> d l13 1-22 bib ab
```

L13 ANSWER 1 OF 22 MEDLINE on STN
AN 2004152998 IN-PROCESS
DN PubMed ID: 15046217
TI Circulating matrix metalloproteinases 1, 2, 9 and their inhibitors TIMP-1 and TIMP-2 as serum markers of **liver fibrosis** in patients with chronic hepatitis C: comparison with PIIINP and hyaluronic acid.
AU Leroy Vincent; Monier Frederique; Bottari Serge; Trocme Candice; Sturm Nathalie; Hilleret Marie-Noelle; Morel Francoise; Zarski Jean-Pierre
CS Departement d 'Hepato-Gastroenterologie, CHU de Grenoble, France.
SO American journal of gastroenterology, (2004 Feb) 99 (2) 271-9.
Journal code: 0421030. ISSN: 0002-9270.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20040330
Last Updated on STN: 20040330
AB OBJECTIVES: Histological examination of liver biopsy is currently required in the management of patients with chronic hepatitis C. Our aim was to evaluate the **diagnostic** utility of a panel of circulating markers in **detecting** the stage of fibrosis. METHODS: One hundred and ninety four-patients who had undergone a percutaneous liver biopsy before antiviral treatment, and 194 age- and sex-matched healthy subjects were studied. Serum levels of hyaluronate, procollagen type III N-terminal peptide (PIIINP), matrix metalloproteinases (MMP)-1, MMP-2, MMP-9 and their tissue inhibitors of metalloproteinases (TIMP)-1 and TIMP-2 were determined by RIA and ELISA. Histological lesions were staged according to the METAVIR score. RESULTS: Hyaluronate, PIIINP, TIMP-1, and TIMP-2 serum levels were significantly higher in patients than in controls. Six markers were significantly correlated with fibrosis: MMP-2 ($r = 0.28$; $p < 0.01$), TIMP-1 ($r = 0.42$; $p < 0.001$), HA ($r = 0.50$; $p < 0.001$), PIIINP ($r = 0.62$; $p < 0.0001$), MMP-1 ($r = -0.32$; $p < 0.01$), and MMP-9 ($r = -0.22$; $p < 0.05$). By multivariate analysis, only PIIINP and MMP-1 were independently associated with fibrosis, and were combined using the equation of the logistic regression model. Using receiver-operating characteristics analysis, the area under the curve of the score to discriminate mild (F0/F1) from significant fibrosis (F2/F3/F4) was 0.82, with a sensitivity of 60% for a specificity of 92%. CONCLUSION: Our results suggest that **combining** two serum **markers** reflecting fibrogenesis (PIIINP) and fibrolysis (MMP-1) may provide a useful tool for evaluating **liver fibrosis**.

L13 ANSWER 2 OF 22 CA COPYRIGHT 2004 ACS on STN
AN 139:242563 CA
TI Macromolecular markers for the **diagnosis** of **liver fibrosis**
IN Rose, Steven L.; Oh, Esther H.; Walsh, Michael J.
PA Prometheus Laboratories, Inc., USA
SO PCT Int. Appl., 133 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PCT corresponding to instant application

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2003073822	A2	20030912	WO 2003-US6038	20030228

W: AE, AG, AL, AM, AT, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EE, EE, ES, FI, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,

ZW, AM, AZ, BY
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003175686 A1 20030918 US 2002-87188 20020228
PRAI US 2002-87188 A 20020228
AB The present invention provides a method of **diagnosing** the presence or severity of **liver fibrosis** in an individual by **detecting** α2-macroglobulin (α2-MG) in sample from the individual; **detecting** hyaluronic acid (HA) in a sample from the individual; **detecting** tissue inhibitor of metalloproteinases-1 (TIMP-1) in a sample from the individual; and **diagnosing** the presence or severity of **liver fibrosis** in the individual based on the presence or level of α2-MG, HA and TIMP-1. A number of liver markers were analyzed in serum of patients with **liver fibrosis** of known stages. Statistical analyses of the ability of a number of **combinations** of **markers** to accurately discriminate the disease are presented.

L13 ANSWER 3 OF 22 MEDLINE on STN
AN 2003587883 MEDLINE
DN PubMed ID: 14669336
TI Relationship between clinical and pathologic findings in patients with chronic liver diseases.
AU Lu Lun-Gen; Zeng Min-De; Mao Yi-Min; Li Ji-Qiang; Qiu De-Kai; Fang Jing-Yuan; Cao Ai-Ping; Wan Mo-Bin; Li Cheng-Zhong; Ye Jun; Cai Xiong; Chen Cheng-Wei; Wang Ji-Yao; Wu Shan-Ming; Zhu Jin-Shui; Zhou Xia-Qiu
CS Shanghai Institute of Digestive Disease, Renji Hospital, Shanghai Second Medical University, Shanghai 200001, China.. lulungen@online.sh.cn
SO World journal of gastroenterology : WJG, (2003 Dec) 9 (12) 2796-800. Journal code: 100883448. ISSN: 1007-9327.
CY China
DT Journal; Article; (JOURNAL ARTICLE) (MULTICENTER STUDY)
LA English
FS Priority Journals
EM 200403
ED Entered STN: 20031216
Last Updated on STN: 20040316
Entered Medline: 20040315
AB AIM: To explore the relationship between clinical findings of patients with chronic liver diseases and the pathologic grading and staging of liver tissues. METHODS: The inflammatory activity and **fibrosis** of consecutive **liver** biopsies from 200 patients were determined according to the **diagnosis** criteria of chronic hepatitis in China established in 1995. A comparative analysis was carried out for 200 patients with chronic liver diseases by comparing their clinical manifestations, serum biochemical markers with the grading and staging of liver tissues. RESULTS: It was revealed that age, index of clinical symptoms and physical signs were obviously relevant to the pathologic grading and staging of liver tissues ($P<0.05$). Blood platelet, red blood cells, aspartate aminotransferase (AST), N-terminal procollagen III (PIII NP) were apparently correlated with the degree of inflammation. PGA (prothrombin time, GGT, apoprotein A1) index, PGAA (PGA+delta2-macroglobulin) index, albumin and albumin/globulin were relevant to both inflammation and fibrosis. Hyaluronic acid (HA) was an accurate variable for the severity of **hepatic** inflammation and **fibrosis**. The **combination** of serum **markers** for fibrosis could increase the **diagnostic** accuracy. It was notable that viral replication markers were not relevant to the degree of inflammation and fibrosis. CONCLUSION: There is a good correlation between clinical findings and the pathologic grading and staging of liver tissues, which

may give aid to the noninvasive **diagnosis** of **liver fibrosis.**

L13 ANSWER 4 OF 22 MEDLINE on STN
AN 2004045128 IN-PROCESS
DN PubMed ID: 14744384
TI **Diagnostic** values of serum levels of HA, PC III, C IV and LN to the **liver fibrosis** in children with beta-thalassemia major.
AU Xu Hong-gui; Fang Jian-pei; Huang Shao-liang; Li Hai-gang; Zhong Feng-yi; Guo Hai-xia; Su Hong
CS Department of Pediatrics, Second Affiliated Hospital, Sun Yat-Sen University, Guangzhou 510120, China.
SO Zhonghua er ke za zhi. Chinese journal of pediatrics, (2003 Aug) 41 (8) 603-6.
Journal code: 0417427. ISSN: 0578-1310.
CY China
DT Journal; Article; (JOURNAL ARTICLE)
LA Chinese
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20040128
Last Updated on STN: 20040309
AB OBJECTIVE: The presence of **liver fibrosis** in patients with beta-thalassemia major has been demonstrated to be an important negative **prognostic** factor. Identification of **liver fibrosis** in early stage would be of great value. Hyaluronic acid (HA), type III pre-collagen (PC III), collagen IV (C IV) and laminin (LN) as serum markers were widely used in the **diagnosis** of **liver fibrosis** in patients with chronic viral infections or alcoholic liver diseases. However, their values in thalassemic **liver fibrosis** have not been studied. This work was to determine the serum HA, PC III, C IV and LN levels in children with beta-thalassemia major and evaluate the **diagnostic** utility. METHOD: Serum HA, PC III, C IV and LN in 49 hospitalized children with beta-thalassemia major (aged 1 - 15 years with the media age of 6.27 years) and 41 healthy children served as controls (aged 1 - 13 years with media age of 6.40 years) were **detected** by radioimmunoassay (RIA). Forty-five of 49 cases were performed percutaneous liver biopsies, and the histopathological fibrosis was compared with the four serum markers. The correlation and discriminate analysis were used. RESULTS: All the serum levels of HA, PC III, C IV and LN in beta-thalassemia were significantly higher than those in controls ($P < 0.01$). In 36 of 45 cases, the histopathology showed **liver fibrosis** including stage I and stage II by biopsies with a positive rate of 80%. The serum levels of four markers increased successively with the aggravation of **liver fibrosis** from stage 0 to stage II, and significant correlation was observed between the level of HA or PC III and the stage of fibrosis (HA, $r = 0.379$, $P = 0.017$; PC III, $r = 0.455$, $P = 0.04$). While there was no difference between the level of C IV or LN and fibrosis (C IV, $r = 0.312$, $P = 0.053$; LN, $r = 0.310$, $P = 0.055$). Using discriminate analysis, the discriminate function of co-**detection** of the four markers for the **diagnosis** of fibrosis was 0.002 HA + 0.003 PC III + 0.002 C IV + 0.006 LN-1.859, which had a sensitivity of 93.88%, specificity of 68.29%, predictive value of positive test and negative test of 77.97% and 90.32%, respectively. Moreover, there was a significant correlation between the serum level of HA or PC III and the liver iron concentration (HA, $r = 0.318$, $P = 0.035$; PC III, $r = 0.305$, $P = 0.044$). CONCLUSION: The results suggest that, in beta-thalassemia major with chronic liver disease, HA and PC III showed more practical value in **diagnosing liver fibrosis** than the levels of C IV and LN. The **combination** of the four serum **markers** could improve the accuracy and reliability of the **diagnosis.** A validation study is necessary

before introducing into the prediction function during the clinical practice.

L13 ANSWER 5 OF 22 CA COPYRIGHT 2004 ACS on STN DUPLICATE 1
AN 139:270330 CA
TI Biochemical surrogate markers of **liver fibrosis** and activity in a randomized trial of peginterferon alfa-2b and ribavirin
AU Poynard, Thierry; McHutchison, John; Manns, Michael; Myers, Rob P.; Albrecht, Janice
CS Service d'Hepato-Gastroenterologie, Groupe Hospitalier Pitie-Salpetriere, Universite Paris VI, Paris, Fr.
SO Hepatology (Philadelphia, PA, United States) (2003), 38(2), 481-492
CODEN: HPTLD9; ISSN: 0270-9139
PB W. B. Saunders Co.
DT Journal
LA English
AB **Liver fibrosis** and activity indexes were validated in patients infected by hepatitis C virus (HCV) nontreated and treated by interferon. The aim was to validate their usefulness as surrogate markers of histol. features using the data of a randomized trial of combination peginterferon alfa-2b and ribavirin. Three hundred fifty-two patients who had 2 interpretable liver biopsies and stored serum sample before and after treatment were selected. Two hundred eight patients received peginterferon alfa-2b 1.5 mcg per kg and ribavirin and 144 patients interferon alfa-2b 3 MU three times a week and ribavirin for 48 wk. A fibrosis and an activity index **combining** 5 and 6 biochem. **markers** were assessed at baseline and at end of follow-up (24 wk after treatment). The biochem. markers have significant predictive values both for the **diagnosis** of fibrosis and for activity. For the **diagnosis** of bridging fibrosis and/or moderate necroinflammatory activity, the area under the receiver operating characteristics curve of the activity index was 0.76±0.03 at baseline and 0.82±0.02 at end of follow-up. A cutoff of activity index at 0.30 (range, 0.00-1.00) had 90% sensitivity and 88% pos. predictive value for the **diagnosis** of bridging fibrosis or moderate necroinflammatory activity. Sensitivity analyses with biopsy specimens of size greater than 15 mm suggest that a part of discordances between biochem. markers and histol. were due to biopsy specimen sampling error. In conclusion, these biochem. markers of fibrosis and activity could be used as surrogate markers for liver biopsy in patients with chronic hepatitis C, both for the initial evaluation and for follow-up.
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 6 OF 22 MEDLINE on STN
AN 2003310269 IN-PROCESS
DN PubMed ID: 12837216
TI Noninvasive evaluation of **liver fibrosis** in chronic hepatitis B patients.
AU Chen Yu; Wang Bao-en; Jia Ji-dong; Qian Lin-xue; Wang Tai-ling; Chen Min-hua; Chen Guang-yong; He Wen; Ding Hui-guo; Yin Shan-shan; Zhang Yan; Dong Zhong
CS Center for Artificial Liver, Beijing You'an Hospital, Affiliated to Capital University of Medical Sciences, Beijing 100054, China.
SO Zhonghua gan zang bing za zhi = Zhonghua ganzangbing zazhi = Chinese journal of hepatology, (2003 Jun) 11 (6) 354-7.
Journal code: 9710009. ISSN: 1007-3418.
CY China
DT Journal; Article; (JOURNAL ARTICLE)
LA Chinese
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20030703
Last Updated on STN: 20031218

AB OBJECTIVE: To investigate the clinical usefulness of noninvasive **diagnostic** methods in evaluating **liver fibrosis** in hepatitis B virus (HBV) patients. METHODS: 102 patients with chronic hepatitis B (CHB) were enrolled from Beijing Friendship Hospital Affiliated to Capital University of Medical Sciences. Noninvasive **diagnostic** methods including ultrasonography, CT, serum markers of **liver** function and **fibrosis**, and HBV DNA were performed and compared with histological fibrotic changes in order to establish a noninvasive method for **detecting** the degree of **liver fibrosis**. RESULTS: The total score of liver surface, edge, parenchyma echogenicity, intrahepatic vessels, and the size of spleen had a coefficient of 0.822 with fibrotic stage. By receiver operating curve (ROC) analysis, the sensitivity to distinguish cirrhosis from CHB was 86.1% and the specificity was 95.5% if the total ultrasonic score was more than 10. The CT imaging **diagnosed** liver cirrhosis with a specificity of 100% and a sensitivity of 48.5%. The change of CT values in cirrhotic patients was lower than that in controls and no cirrhotic patients ($F=5.805$, $P<0.01$), when the voltage was increased from 100 KV to 140 KV. Except normal controls and S1 group, S2 and S3 group, the level of HA and collagen IV between the other groups were statistically different. The cut-off value of HA to **diagnose** cirrhosis was 108 (microg/L) with a sensitivity of 72.2% and a specificity of 80.3%. The cut-off value of collagen IV to **diagnose** cirrhosis was 188 (microg/L) with a sensitivity of 72.2% and a specificity of 78.8%. When ultrasonography was **combined** with serum **markers**, the sensitivity was 72.2% and the specificity was 80.3%. CONCLUSION: Both ultrasonography and serum markers are useful to **diagnose** cirrhosis. The combination of the two examinations is more valuable than any one alone. The characteristic CT imaging has high specificity but low sensitivity in **diagnosing** early cirrhosis. HA and collagen IV are correlated more closely with the stage of fibrosis, and can reflect the severity of fibrosis.

L13 ANSWER 7 OF 22 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 2
AN 2003:237603 BIOSIS
DN PREV200300237603
TI Determination of serum fibrosis indexes in patients with chronic hepatitis and its significance.
AU Zheng Min; Cai Weimin [Reprint Author]; Weng Honglei; Liu Ronghua
CS Institute of Infectious Diseases, First Affiliated Hospital, Zhejiang University School of Medicine, Hangzhou, 310003, China
caiweimin_hz@hotmail.com
SO Chinese Medical Journal (English Edition), (March 2003) Vol. 116, No. 3, pp. 346-349. print.
CODEN: CMJODS. ISSN: 0366-6999.
DT Article
LA English
ED Entered STN: 14 May 2003
Last Updated on STN: 14 May 2003

post-dates

AB Objectives: To study the relationship between serum levels of hyaluronic acid (HA), type III procollagen (PC III), laminin (LN), type IV collagen (IV-C) and **hepatic fibrosis** and to determine their value in clinical practice. Methods: 2600 serum samples from chronic hepatitis patients were assayed for fibrosis indexes including HA, PC III, LN and IV-C with RIA. Liver biopsy was performed in 280 of those patients and the biopsy material was examined histopathologically. The inflammation grade of the **liver**, stage of **fibrosis** and degree of chronic hepatitis were recorded and were compared with fibrotic indexes. Results: Among 2600 chronic hepatitis patients, every fibrotic index had a significant correlation with the inflammation grade, fibrosis staging and the degree of chronic hepatitis ($P<0.01$). The coefficient correlation of the results of histopathological examinations to HA was

0.544, 0.548 and 0.468 respectively, that to PC III, 0.495, 0.424 and 0.335, that to LN, 0.214, 0.204 and 0.184, and that to IV-C, 0.406, 0.404 and 0.412, respectively. Conclusions: Serum fibrosis indexes are fairly well correlated with the inflammation grade of the **liver**, **fibrosis** staging and the degree of chronic hepatitis. However, as **diagnostic markers**, they should be considered in **combination** with liver function tests, ultrasonography and clinical manifestations.

L13 ANSWER 8 OF 22 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2003:580493 BIOSIS
DN PREV200300571161
TI NON-INVASIVE MARKERS OF FIBROTIC NONALCOHOLIC STEATOHEPATITIS.
AU Oh, Sangik [Reprint Author]; Benson, Aaron [Reprint Author]; Grossman, Joseph [Reprint Author]; Nasser, Imad [Reprint Author]; Curry, Michael P. [Reprint Author]; Afdhal, Nezam H. [Reprint Author]
CS Boston, MA, USA
SO Digestive Disease Week Abstracts and Itinerary Planner, (2003) Vol. 2003, pp. Abstract No. M1376. e-file.
Meeting Info.: Digestive Disease 2003. FL, Orlando, USA. May 17-22, 2003. American Association for the Study of Liver Diseases; American Gastroenterological Association; American Society for Gastrointestinal Endoscopy; Society for Surgery of the Alimentary Tract.
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LA English
ED Entered STN: 10 Dec 2003
Last Updated on STN: 10 Dec 2003
AB BACKGROUND: The challenge for the clinician in assessing the patients with nonalcoholic fatty liver disease (NAFLD) is to differentiate those with steatosis alone from those with progressive liver disease. At the present time, liver biopsy remains as the gold standard in staging **hepatic fibrosis**. OBJECTIVES: To assess the role of serum YKL-40 and HA in differentiating patients with fibrotic nonalcoholic steatohepatitis(NASH) from those with simple steatosis. METHODS: We performed a cross sectional analysis of 60 consecutive patients with NAFLD. Various clinical and biochemical data were obtained including estimation of insulin resistance by using homeostasis model assessment (HOMA). Serum levels of YKL-40 and HA were measured by ELISA and compared to histological staging of biopsies by Brunt Score and Computerized Image Analysis. RESULTS: Thirty-one patients had simple steatosis and 29 patients were found to have steatosis plus fibrosis. Our univariate analysis showed that the fibrosis group consisted of more diabetics (21.7% vs. 0%, p=0.02), higher insulin resistance based on HOMA index (5.99 vs. 3.47, p=0.01) and higher AST/ALT ratio (0.73 vs. 0.55, p= 0.01). There were no significant differences in mean age, number of females, body mass index (BMI) and total cholesterol levels between the two groups. The mean of serum YKL-40 was significantly higher (142 vs 72 ng/ml, $p < 0.05$) in patients with fibrosis (stage 1-4) than simple steatosis. There was a trend towards higher serum levels of hyaluronic acid in the fibrosis group (61 vs. 36.3 U/ml, p=0.06) but this did not reach statistical significance with current sample size. However, when we compared simple steatosis to stage 2 to 4 fibrosis, both serum markers were significantly higher in the fibrosis group. A receiver operator curve (ROC) curve for serum YKL-40 revealed a sensitivity of 75% and a specificity of 90% in **detecting** fibrosis stage greater than or equal to Stage 2 when cutoff concentration was 116 ng/ml. Hyaluronic acid had sensitivity of 50% and specificity of 95% in **detecting** patients with fibrosis stage greater than or equal to Stage 2 when cutoff concentration was 84.6 U/ml. When two serum fibrosis **markers** are **combined** to **detect** fibrosis stage greater than or equal to 2, the sensitivity was 100% and specificity was 50%. CONCLUSIONS: Serum YKL-40 and HA are

useful markers in differentiating patients with simple steatosis from NASH patients with fibrosis stage greater than or equal to 2. In association with clinical parameters, they may identify suitable patients for liver biopsy.

L13 ANSWER 9 OF 22 CA COPYRIGHT 2004 ACS on STN DUPLICATE 3
AN 138:87746 CA
TI Biochemical markers of **liver fibrosis**: a comparison with historical features in patients with chronic hepatitis C
AU Myers, Robert P.; Ratziu, Vlad; Imbert-Bismut, Francoise; Charlotte, Frederic; Poynard, Thierry
CS MULTIVIRC Group, Departments of Hepato-Gastroenterology, Biochemistry, and Pathology, Hopital La Pitie-Salpetriere, Paris, Fr.
SO American Journal of Gastroenterology (2002), 97(9), 2419-2425
CODEN: AJGAAR; ISSN: 0002-9270
PB Elsevier Science Inc.
DT Journal
LA English
AB **Liver fibrosis** in chronic hepatitis C is related to sex, age at infection, duration of infection, and alc. consumption. Several noninvasive biochem. markers are highly predictive for the discrimination of significant fibrosis. The aims of this study were: (1) to compare an index of five biochem. markers with historical features; and (2) to determine the utility of **combining** these features with the five-**marker** index for the prediction of significant fibrosis. Untreated patients with chronic hepatitis C and a known duration of infection had a liver biopsy and serum tested for markers of fibrosis. The discriminative values of the markers and an index of historical features for the **diagnosis** of clin. significant fibrosis (F2-F4 by the Metavir system) were compared using areas under receiver operating characteristic (ROC) curves. A modified index was constructed **combining** the five-**marker** index and historical features. A total of 211 patients were included. Of these, 52% were male, and 19% consumed ≥50 g of alc. daily. The median age at infection was 28±13 yr and the median duration of infection was 17±8 yr (range 1-48 yr). By multivariate logistic regression anal., sex ($p = 0.003$), age at biopsy ($p = 0.004$), and alc. consumption ($p = 0.042$) were independently predictive of F2-F4 fibrosis. For the discrimination of F2-F4 fibrosis, the areas under the ROC curves were 0.796±0.033 for the five-marker index vs. 0.709±0.037 for the historical index ($p = 0.079$). For **diagnosis** of advanced fibrosis (F3 and F4), the areas under the curves were 0.920±0.032 and 0.762±0.049 ($p = 0.007$), resp. The discriminative value of the combined biochem. and historical index was not statistically significantly different from that of the five-marker index alone (p = ns). A simple index including age, sex, and five biochem. markers accurately predicts significant hepatitis C-related fibrosis. This index is more accurate than an index of historical features, the addition of which to the existing index was not helpful.
RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 10 OF 22 MEDLINE on STN
AN 2002640839 MEDLINE
DN PubMed ID: 12395328
TI Quantitative evaluation of altered hepatic spaces and membrane transport in **fibrotic** rat **liver**.
AU Hung Daniel Y; Chang Ping; Cheung Kee; Winterford Clay; Roberts Michael S
CS Department of Medicine and Division of Chemical Pathology, University of Queensland, Princess Alexandra Hospital, Woollongabba, Australia.
SO Hepatology (Baltimore, Md.), (2002 Nov) 36 (5) 1180-9.
Journal code: 8302946. ISSN: 0270-9139.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS Priority Journals
EM 200212
ED Entered STN: 20021026
Last Updated on STN: 20021217
Entered Medline: 20021209
AB Four animal models were used to quantitatively evaluate hepatic alterations in this study: (1) a carbon tetrachloride control group (phenobarbital treatment only), (2) a CCl(4)-treated group (phenobarbital with CCl(4) treatment), (3) an alcohol-treated group (liquid diet with alcohol treatment), and (4) a pair-fed alcohol control group (liquid diet only). At the end of induction, single-pass perfused livers were used to conduct **multiple indicator** dilution (MID) studies.
Hepatic spaces (vascular space, extravascular albumin space, extravascular sucrose space, and cellular distribution volume) and water hepatocyte permeability/surface area product were estimated from nonlinear regression of outflow concentration versus time profile data. The hepatic extraction ratio of (3)H-taurocholate was determined by the nonparametric moments method. Livers were then dissected for histopathologic analyses (e.g., fibrosis index, number of fenestrae). In these 4 models, CCl(4)-treated rats were found to have the smallest vascular space, extravascular albumin space, (3)H-taurocholate extraction, and water hepatocyte permeability/surface area product but the largest extravascular sucrose space and cellular distribution volume. In addition, a linear relationship was found to exist between histopathologic analyses (fibrosis index or number of fenestrae) and hepatic spaces. The hepatic extraction ratio of (3)H-taurocholate and water hepatocyte permeability/surface area product also correlated to the severity of fibrosis as defined by the fibrosis index. In conclusion, the **multiple indicator** dilution data obtained from the in situ perfused rat liver can be directly related to histopathologic analyses.

L13 ANSWER 11 OF 22 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2002:378564 BIOSIS
DN PREV200200378564
TI Cationic drug pharmacokinetics in diseased **livers** determined by **fibrosis** index, **hepatic** protein content, microsomal activity, and nature of drug.
AU Hung, Daniel Y.; Chang, Ping; Cheung, Kee; McWhinney, Brett; Masci, Paul P.; Weiss, Michael; Roberts, Michael S. [Reprint author]
CS Department of Medicine, University of Queensland, Princess Alexandra Hospital, Woollongabba, QLD, 4102, Australia
M.Roberts@mailbox.uq.edu.au
SO Journal of Pharmacology and Experimental Therapeutics, (June, 2002) Vol. 301, No. 3, pp. 1079-1087. print.
CODEN: JPETAB. ISSN: 0022-3565.
DT Article
LA English
ED Entered STN: 10 Jul 2002
Last Updated on STN: 10 Jul 2002
AB The disposition kinetics of six cationic drugs in perfused diseased and normal rat livers were determined by **multiple indicator** dilution and related to the drug physicochemical properties and liver histopathology. A carbon tetrachloride (CCl4)-induced acute hepatocellular injury model had a higher fibrosis index (FI), determined by computer-assisted image analysis, than did an alcohol-induced chronic hepatocellular injury model. The alcohol-treated group had the highest hepatic alpha1-acid glycoprotein, microsomal protein (MP), and cytochrome P450 (P450) concentrations. Various pharmacokinetic parameters could be related to the octanol-water partition coefficient (log Papp) of the drug as a surrogate for plasma membrane partition coefficient and affinity for MP or P450, the dependence being lower in the CCl4-treated group and higher in the alcohol-treated group relative to controls. Stepwise

regression analysis showed that hepatic extraction ratio, permeability-surface area product, tissue-binding constant, intrinsic clearance, partition ratio of influx (kin) and efflux rate constant (kout), and kin/kout were related to physicochemical properties of drug (log Papp or pKa) and liver histopathology (FI, MP, or P450). In addition, hepatocyte organelle ion trapping of cationic drugs was evident in all groups. It is concluded that **fibrosis**-inducing **hepatic** disease effects on cationic drug disposition in the liver may be predicted from drug properties and liver histopathology.

L13 ANSWER 12 OF 22 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2002:345938 BIOSIS
DN PREV200200345938
TI Could biochemical markers of **liver fibrosis** reduce the number of liver biopsies?.
Original Title: Biopsie du foie contre prise de sang pour le suivi de l'hepatite C?.
AU Poynard, Thierry [Reprint author]; Ratziu, Vlad [Reprint author]; Moussalli, Joseph [Reprint author]; Regimbeau, Corinne [Reprint author]; di Martino, Vincent [Reprint author]; Benhamou, Yves [Reprint author]; Myers, Rob [Reprint author]; Imbert-Bismut, Francoise [Reprint author]
CS Service d'hepatogastroenterologie, Service de Biochimie, Groupe MULTIVIRC, Groupe Hospitalier Pitie-Salpetriere, 47, Boulevard de l'Hopital, 75651, Paris Cedex 13, France
SO M-S (Medecine Sciences), (Mars, 2002) Vol. 18, No. 3, pp. 353-356. print.
ISSN: 0767-0974.
DT Article
LA French
ED Entered STN: 19 Jun 2002
Last Updated on STN: 19 Jun 2002
AB Liver biopsy is actually essential for the management of patients infected by hepatitis C virus. It is necessary to grade and stage hepatitis and fibrosis, and make decision about treatment. However, liver biopsy is aggressive and can be a limitation for patients management. With a **combination** of five basic serum biochemical **markers** for **diagnosis** of fibrosis, high positive and negative predictive values of important fibrosis can be obtained, suggesting that this index of fibrosis could be used to substantially reduce the number of liver biopsies.

post dates but close

L13 ANSWER 13 OF 22 MEDLINE on STN
AN 2002241582 MEDLINE
DN PubMed ID: 11876795
TI Biochemical markers of **liver fibrosis** in patients infected by hepatitis C virus: longitudinal validation in a randomized trial.
AU Poynard T; Imbert-Bismut F; Ratziu V; Chevret S; Jardel C; Moussalli J; Messous D; Degos F
CS Hepatogastroenterology Groupe Hospitalier Pitie-Salpetriere, 47 Boulevard de l'Hopital, 75651 Paris Cedex 13, France. (GERMED cyt04 group).
tpoynard@teaser.fr
SO Journal of viral hepatitis, (2002 Mar) 9 (2) 128-33.
Journal code: 9435672. ISSN: 1352-0504.
CY England: United Kingdom
DT (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LA English
FS Priority Journals
EM 200206
ED Entered STN: 20020501
Last Updated on STN: 20020604

post dates but this would be in Feb if came out of record on 1449

need to check date

Entered Medline: 20020603

AB A **liver fibrosis** index was recently prospectively validated in a cross-sectional study where patients infected by hepatitis C virus (HCV) had only one biopsy and no longitudinal follow-up. The aim of this study was to retrospectively assess the **diagnostic** value of this index in patients included in a randomized trial of interferon (IFN) using repeated measurements, two biopsies and hyaluronic acid as a comparative reference. One-hundred and sixty-five patients who had had two interpretable liver biopsies and at least one stored serum sample before IFN treatment were selected. Seventy-eight patients received 3 MU of IFN-alpha thrice weekly for 24 weeks and 87 followed a reinforced regimen for 48 weeks. A fibrosis index **combining** five biochemical **markers** (alpha2-macroglobulin, haptoglobin, apolipoprotein A1, gamma-glutamyl transpeptidase (GGT) and total bilirubin adjusted for gender and age) as well as hyaluronic acid was assessed on 461 samples available at baseline, at the end of treatment and at the end of follow-up (72 weeks).There was a significant decrease of the fibrosis index score among the 17 sustained virologic responders, from 0.33 +/- 0.06 (mean +/- SE) at baseline to 0.18 +/- 0.06 at 72 weeks in comparison with 92 nonresponders (from 0.41 +/- 0.03 at baseline to 0.44 +/- 0.03 at 72 weeks; $P < 0.001$) and in comparison with 56 relapsers (from 0.36 +/- 0.03 at baseline to 0.32 +/- 0.03 at 72 weeks; $P=0.05$). No significant differences were observed for hyaluronic acid.Hence, this fibrosis index could be used as a surrogate marker of the antifibrotic effect of treatments in patients with chronic hepatitis C.

L13 ANSWER 14 OF 22 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
AN 2004:47779 BIOSIS
DN PREV200400050027
TI Evaluation of **liver fibrosis** by **combined** serum **markers** in chronic hepatitis C patients treated by interferon alpha and ribavrin.
AU Leroy, Vincent [Reprint Author]; Trocme, Candice; Bottari, Serge; Sturm, Nathalie; Morel, Francoise; Zarski, Jean-Pierre [Reprint Author]
CS Department of Hepatogastroenterology, CHU Grenoble, Grenoble, France
SO Journal of Hepatology, (April 2002) Vol. 36, No. Supplement 1, pp. 116. print.
Meeting Info.: Biennial Meeting of the International Association for the Study of the Liver. Madrid, Spain. April 15-16, 2002. European Association for the Study of the Liver; International Association for the Study of the Liver.
ISSN: 0168-8278 (ISSN print).
DT Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LA English
ED Entered STN: 21 Jan 2004
Last Updated on STN: 21 Jan 2004

post dates

L13 ANSWER 15 OF 22 CA COPYRIGHT 2004 ACS on STN DUPLICATE 4
AN 135:316782 CA
TI Biochemical markers of **liver fibrosis** in patients with hepatitis C virus infection: a prospective study
AU Imbert-Bismut, F.; Ratziu, V.; Pieroni, L.; Charlotte, F.; Benhamou, Y.; Poynard, T.
CS The MULTIVIRC Group, Laboratoire d'Immunologie des Tumeurs, Faculte des Sciences Pharmaceutiques et Biologiques de Paris, Department of Biochemistry, Universite Rene Descartes, Paris, 75651, Fr.
SO Lancet (2001), 357(9262), 1069-1075
CODEN: LANCAO; ISSN: 0140-6736
PB Lancet Ltd.
DT Journal
LA English

of record on 1/4/5

AB Liver biopsy is thought mandatory for management of patients with hepatitis C virus (HCV) infection, especially for staging fibrosis. We aimed, in our prospective study, to assess the predictive value of a **combination** of basic serum biochem. **markers** for **diagnosis** of clin. significant fibrosis (including early stages). We assessed liver-biopsy patients with **detectable** HCV by PCR, for eligibility, and took a blood sample on the day of the procedure. The anal. was done in a 1st-year period for 205 patients and then tested in a second period on 134 patients. We devised a fibrosis index that included the most informative **markers** (**combined** with age and sex) for the 1st-year group. 11 Serum markers were assessed as well as fibrosis stage: F0=no fibrosis and F1=portal fibrosis; and for clin. significant fibrosis, F2=few septa, F3=many septa, and F4=cirrhosis. Statistical anal. was by logistic regression, neural connection, and receiver-operating characteristic (ROC) curves. First-year and 2nd-year patient-group characteristics and biochem. markers did not differ. The overall frequency of clin. significant fibrosis was 40% (138 patients). The most informative markers were: α2 macroglobulin, α2 globulin (or haptoglobin), γ globulin, apolipoprotein A1, γ glutamyltranspeptidase, and total bilirubin. The areas (SD) under the ROC curves for the 1st-year (0·836 [0·430]) and 2nd-year groups (0·870 [0·340]) did not differ (p=0·44). With the best index, a high neg. predictive value (100% certainty of absence of F2, F3, or F4) was obtained for scores ranging from 0 to 0·10 (12% [41] of all patients), and high pos. predictive value (>90% certainty of presence of F2, F3, or F4) for scores ranging from 0·60 to 1·00 (34% [115] of all patients). A **combination** of basic serum **markers** could be used to substantially reduce the number of liver biopsies done in patients with chronic HCV infection.

RE.CNT 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 16 OF 22 MEDLINE on STN
AN 2002073097 MEDLINE
DN PubMed ID: 11798612
TI Determination and significance of serum markers for fibrosis in patients with chronic hepatitis.
AU Cai W; Zheng M; Weng H; Liu R
CS The Institute of Infectious Diseases, The First Affiliated Hospital, School of Medicine, Zhejiang University, Hangzhou 310003, China.
SO Zhonghua nei ke za zhi [Chinese journal of internal medicine], (2001 Jul) 40 (7) 448-51.
Journal code: 16210490R. ISSN: 0578-1426.
CY China
DT Journal; Article; (JOURNAL ARTICLE)
LA Chinese
FS Priority Journals
EM 200309
ED Entered STN: 20020125
Last Updated on STN: 20021211
Entered Medline: 20030923

inconclusive with respect to amounts these markers

AB OBJECTIVE: To find the relationship between serum levels of hyaluronic acid (HA), type III procollagen (PC III), laminin (LN), type IV collagen (IV-C) and **hepatic fibrosis** as well as to determine their value in clinical practice. METHODS: 2600 serum samples from chronic hepatitis patients were tested with RIA for fibrosis indexes assays including HA, PC III, LN and IV-C. 280 of the patients with serum samples taken had liver biopsy performed and the biopsy material was examine pathomorphologically. Fibrosis indexes were compared according to inflammation grade, fibrosis stage and chronic hepatitis degree. RESULTS: In the 2600 serum samples from chronic hepatitis patients, fibrosis indexes (including HA, PC III, LN and IV-C) had significant correlation with inflammation grade, fibrosis stage and the degree of chronic

hepatitis (P < 0.01). The relating indexes to HA were 0.544, 0.548, 0.468 respectively, to PC III 0.495, 0.424, 0.335 respectively, to LN 0.214, 0.204, 0.184 and to IV-C were 0.464, 0.404, 0.412 respectively. CONCLUSION: Serum fibrosis indexes are fairly well correlated with the inflammation grade, fibrosis stage and the degree of chronic hepatitis. However, as **diagnostic markers**, they must be **combined** with liver function, ultrasonography and clinical features.

L13 ANSWER 17 OF 22 CA COPYRIGHT 2004 ACS on STN
AN 136:384107 CA
TI Relationships between serum markers of **liver fibrosis** and pathological changes in chronic hepatitis
AU Ren, Weiying; Zhang, Shuncai; Hu, Dechang; Liu, Houyu
CS Department of Gastroenterology, Zhongshan Hospital, Fudan University, Shanghai, 200032, Peop. Rep. China
SO Fudan Xuebao, Yixue Kexueban (2001), 28(4), 343-346
CODEN: FXYKAS
PB Shanghai Yike Daxue Chubanshe
DT Journal
LA Chinese
AB The relationship between serum markers of **liver fibrosis** and pathol. changes in chronic hepatitis was studied. Serum levels of precollagen type III peptide (PIII P), collagen type IV (CIV), and hyaluronic acid (HA) were **detected** by RIA (RIA) or enzyme linked immunosorbent assay (ELISA) in 243 patients with chronic liver disease. The pathol. changes of liver biopsy were described as stage for fibrosis extent and grade for inflammation activity. The stage and grade were interrelated. The serum levels of PIII P, CIV, and HA were increased with the progress of **liver fibrosis**, and were pos. correlated with the fibrotic stage and grade. The sensitivity and specificity for **diagnosis** of **liver fibrosis** with **combination** of the three **markers** were 88.7% and 71.4%, resp. Only the level of HA in 12 patients with liver cirrhosis was significantly higher than that with chronic hepatitis stage 4 (P <0.05). The results showed that serum PIII P, CIV, and HA may be used for assessing the extent of **liver fibrosis**, and inflammation may play an important role in fibrogenesis.

L13 ANSWER 18 OF 22 MEDLINE on STN
AN 2002006858 MEDLINE
DN PubMed ID: 11177689
TI **Hepatic fibrosis**: are any of the serum markers useful?.
AU Oh S; Afdhal N H
CS Beth Israel Deaconess Medical Center, Harvard Medical School, 110 Francis Street, Suite 8E, Boston, MA 02215, USA.
SO Current gastroenterology reports, (2001 Feb) 3 (1) 12-8. Ref: 52
Journal code: 100888896. ISSN: 1522-8037.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200310
ED Entered STN: 20020121
Last Updated on STN: 20021211
Entered Medline: 20031031
AB There is a clinical need for noninvasive measurement of **liver fibrosis** both to **diagnose** significant **liver fibrosis** and to **monitor** the effects of therapy on fibrogenesis and fibrolysis. **Multiple** clinical **markers**

Hard copy ordered from STIC on 4/23/04 checked 4/26/04

have been evaluated over the years, and as our understanding of the molecular process of liver scarring has advanced, newer markers have appeared. Serum markers include extracellular matrix proteins such as the N-terminal propeptide of collagen III, hyaluronan, YKL-40, laminin, metalloproteinases, and their inhibitors. Use of **multiple markers** has led to 90% sensitivity in **diagnosing** cirrhosis, but specificity is variable at about 60%. Automated systems to measure these markers are under development and are being evaluated for their ability to **monitor** fibrosis during and after therapy in multiple liver diseases, including hepatitis B and C. Although no individual fibrosis marker is clinically applicable today, we foresee a future in which **monitoring** fibrosis markers will replace sequential liver biopsy as a standard of care.

L13 ANSWER 19 OF 22 CA COPYRIGHT 2004 ACS on STN DUPLICATE 5
AN 133:204910 CA
TI Triple-staining to identify apoptosis of hepatic cells in situ
AU Zhang, Jing; You, Honh; Wang, Tailing; Wang, Baoen; Jia, Jidong; Katayama, Hironori; Maeda, Shotaro; Wang, Ruojaio; Asano, Goro; Ishiwata, Toshiyuki; Naito, Zenya; Yokoyama, Munehiro
CS Div Pathol., China-Japan Friendship Hosp., Beijing, 100029, Peop. Rep. China
SO Journal of Nippon Medical School (2000), 67(4), 280-283
CODEN: JNMSF5; ISSN: 1345-4676
PB Medical Association of Nippon Medical School
DT Journal
LA English
AB To identify apoptosis of non-parenchymal cells in **fibrotic livers,** we established a triple staining method which **combined** immunohistochem. for cell **markers** and Masson staining for collagen as well as terminal deoxynucleotidyl transferase UTP nick end labeling (TUNEL). Five μm formalin fixed, paraffin-embedded liver sections were prepared for staining. Firstly, TUNEL staining was carried out to **detect** apoptosis of liver cells. Then, the sections were subjected to immunohistochem. for α-smooth muscle actin (α-SMA) or KP-1 to identify hepatic stellate cells or Kupffer cells. Finally, Masson staining was performed to show the relationship between apoptosis and collagens. In addition, we optimized different conditions of fixation, digestion, and color development which may affect the results.

L13 ANSWER 20 OF 22 CA COPYRIGHT 2004 ACS on STN DUPLICATE 6
AN 128:138283 CA
TI Urinary assays for desmosine and hydroxylysylpyridinoline in the **detection** of cirrhosis
AU Afdhal, Nezam H.; Keaveny, Andrew P.; Cohen, Teven B.; Nunes, David P.; Maldonado, Norris; O'Brien, Michael; Stone, Phillip J.
CS Section of Gastroenterology, Evans Department of Medicine and Thorndike Memorial Laboratories, Boston University School of Medicine, USA
SO Journal of Hepatology (1997), 27(6), 993-1002
CODEN: JOHEEC; ISSN: 0168-8278
PB Munksgaard International Publishers Ltd.
DT Journal
LA English
AB Non-invasive markers of **liver fibrosis** have great potential for both the **diagnosis** and therapy of liver disease and cirrhosis. The aim of this study was to evaluate the potential of urinary amino acids desmosine (DES) and isodesmosine (IDES) derived from the breakdown of elastin and hydroxylysylpyridinoline (HP) and lysylpyridinoline (LP) derived from fibrillar collagen in **diagnosing** chronic liver disease. We studied 48 patients with chronic liver disease who had varying degrees of **liver fibrosis,** graded 0-6 using a modified Knodell score, and 20

control subjects without liver disease. Urinary DES (μg/g creatinine) and HP (nmol/mmol creatinine) were measured by an isotope dilution, high performance liquid chromatog. method. For liver disease patients, aminoterminal propeptide of type III procollagen (PIIINP) and alanine aminotransferase were determined The urine and serum markers were correlated to degree of fibrosis and inflammation on liver biopsies. Differences between groups were analyzed by ANOVA and multiple linear regression was applied to T determine independence of variables. Sensitivity, specificity and receiver operating curves were derived for each marker. In the 17 patients with **liver fibrosis** score of 5-6, mean urinary DES, IDES, HP and LP were all significantly greater than in the control group ($p<0.05$). Urinary DES and IDES correlated best with fibrosis score, $r=0.61$ for both markers. The correlation coefficient between serum PIIINP and fibrosis score was 0.47. Urinary DES and HP each had an overall **diagnostic** accuracy of 77% for fibrosis. **Combining markers** improved accuracy to over 80%. No correlation was seen between the urinary markers and inflammation scores. Urinary DES and HP are potentially useful clin. markers for **liver fibrosis**, especially when used in combination or in association with PIIINP.

RE.CNT 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L13 ANSWER 21 OF 22 CA COPYRIGHT 2004 ACS on STN
AN 120:210564 CA
TI Effect of chronic alcohol intake on rat liver microcirculation assessed by the **multiple indicator** dilution technique
AU Akamatsu, Kouichi; Nishinobu, Masao; Ohuchi, Takashi; Tada, Kouji; Ohta, Yasuyuki
CS Med. Sch., Ehime Univ., Onsen, 791-02, Japan
SO Alcohol and Alcoholism (Oxford, United Kingdom) (1993), 28(1A), 53-8
CODEN: ALALDD; ISSN: 0735-0414
DT Journal
LA English
AB To study the hepatic microcirculatory disturbance in alc. liver injury, rats were chronically (8-12 wk) fed with alc. via a gastric fistula according to the method of Tsukamoto and French (1986). The hepatic microcirculation was studied by measuring the sinusoidal volume (SV) and the apparent space of Disse (DS) volume using a **multiple-indicator** dilution technique. Both the SV and the DS volume were significantly decreased in the alc.-fed rats at 8-12 wk despite the absence of microscopically **detectable hepatic fibrosis**. Similar changes were noted in the alc.-fed and control rats regarding expansion of the SV and the DS volume with alternations in portal pressure. However, since the vols. in the alc.-fed group increased with the increase of portal pressure, they maintained a steady difference from the control values. These results suggest that the decrease of the SV and the DS vl. may have been secondary to compression caused by steatosis and/or hepatocyte enlargement, although a possible role for microscopically undetectable **hepatic fibrosis** could not be ruled out.

L13 ANSWER 22 OF 22 MEDLINE on STN
AN 94190367 MEDLINE
DN PubMed ID: 8141923
TI Effect of chronic alcohol intake on rat liver microcirculation assessed by the **multiple indicator** dilution technique.
AU Akamatsu K; Nishinobu M; Ohuchi T; Tada K; Ohta Y
CS Third Department of Internal Medicine, Ehime University, Medical School, Japan.
SO Alcohol and alcoholism (Oxford, Oxfordshire). Supplement, (1993) 1A 53-8.
Journal code: 8804836. ISSN: 1358-6173.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)

LA English
FS Priority Journals
EM 199404
ED Entered STN: 19940511
Last Updated on STN: 19970203
Entered Medline: 19940429
AB To study the hepatic microcirculatory disturbance in alcoholic liver injury, rats were chronically (8-12 weeks) fed with alcohol via a gastric fistula according to the method of Tsukamoto and French (1986). The hepatic microcirculation was studied by measuring the sinusoidal volume (SV) and the apparent space of Disse (DS) volume using a **multiple -indicator** dilution technique. Both the SV and the DS volume were significantly decreased in the alcohol-fed rats at 8-12 weeks despite the absence of microscopically **detectable hepatic fibrosis**. Similar changes were noted in the alcohol-fed and control rats regarding expansion of the SV and the DS volume with alterations in portal pressure. However, since the volumes in the alcohol-fed group increased with the increase of portal pressure, they maintained a steady difference from the control values. These results suggested that the decrease of the SV and the DS volume may have been secondary to compression caused by steatosis and/or hepatocyte enlargement, although a possible role for microscopically undetectable **hepatic fibrosis** could not be ruled out.

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